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POSTOBSTRUCTIVE NEGATIVE PRESSURE PULMONARY OEDEMA IN A DOG

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Keywords:	Anaesthesia, negative pressure pulmonary oedema, brachycephalic, Intensive care, postobstructive pulmonary oedema, post-anaesthetic complications
Topics:	Anaesthesia and analgesia, Physiology, Imaging

Abstract:	A four-month-old English bulldog was anaesthetised for investigation and management of chronic urinary incontinence. In the post-anaesthetic period the patient developed respiratory distress, with marked cough and increased inspiratory effort. Diagnostic imaging suggested pulmonary oedema. After excluding all other causes of cardiogenic and non-cardiogenic pulmonary oedema it was indicated that the patien developed post-anaesthetic negative pressure pulmonary oedema due to tracheal intubation with an oversized endotracheal tube leading to laryngeal swelling and obstruction. The animal was treated with ox supplementation, corticosteroids and β-2 adrenergic receptor agoni The patient recovered from the event and was discharged from the hospital after forty-eight hours. This article discusses this case in further detail including other management options of negative pressure pulmonary oedema. This is the first case report focused on the pathophysiology, critical care and management of post-anaesthetic negative pressure pulmonary oedema in a dog.

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TITLE OF CASE ***Do not include "a case report"***
POSTOBSTRUCTIVE NEGATIVE PRESSURE PULMONARY OEDEMA IN A DOG
SUMMARY ***Up to 150 words summarising the case presentation and outcome (this will be freely available online)***

A four-month-old English bulldog was anaesthetised for investigation and management of chronic urinary incontinence. In the post-anaesthetic period the patient developed respiratory distress, with marked cough and increased inspiratory effort. Diagnostic imaging suggested pulmonary oedema. After excluding all other causes of cardiogenic and non-cardiogenic pulmonary oedema it was hypothesised that the patient developed postanaesthetic negative pressure pulmonary oedema, suspected to have been exacerbated by tracheal intubation with an oversized endotracheal tube leading to laryngeal swelling and obstruction. The animal was treated with oxygen supplementation, corticosteroids and β-2 adrenergic receptor agonists. The patient recovered from the event and was discharged from the hospital after forty-eight hours. This article discusses in further details other management options of negative pressure pulmonary oedema. This is the first case report discussing the pathophysiology, critical care and management of post-anaesthetic negative pressure pulmonary oedema in a dog.

BACKGROUND ***Why you think this case is important – why did you write it up?***

Pulmonary oedema is defined as an abnormal accumulation of fluid in the extravascular tissues and spaces of the lung that occurs when the lymphatic circulation is unable to drain the excessive fluid present in the extravascular space [1].

Post-obstructive pulmonary oedema can be subdivided into two types: Type 1 ~~which~~ is associated with an increase in inspiratory effort due to an acute upper airway obstruction (UAO) and type 2 ~~which~~ results from ~~a~~ the relief of a chronic partial UAO (e.g. after laryngeal mass resection) [2]. Post-obstructive pulmonary oedema type 1 is also known as negative pressure pulmonary oedema (NPPO) and has been highlighted as a potential complication in the post-anaesthetic period in people and horses[3,4]. Multiple causes have been attributed to the development of NPPO: brachycephalic obstructive airway syndrome (BOAS), strangulation, choking, near drowning, airway collapse, laryngeal mass, laryngeal paralysis, endotracheal tube (ETT) obstruction, laryngospasm and partial occlusion of the upper airway tract with a foreign body or other mass [2,5]. The pathophysiologic mechanism behind NPPO was primarily described in the 1940s [6] and it is now accepted that this is a multifactorial process involving negative pressures and hypoxia[2]. Physiologically the UAO creates a large negative transpulmonary and interpleural pressure gradient favouring movement of fluid from the capillaries ~~through the alveolar capillary barrier~~ into the extravascular space [3]. ~~This increase in hydrostatic pressures and oedema formation in the lungs [2,7], contributes to the~~ leading to lung tissue oedema and the overall translocation of fluid ~~from the capillaries~~ into the alveolar spaces.

In the veterinary literature few reports have been published discussing this event. In 1927, a research article reporting the response to respiratory resistance in dogs found that a partial fixed obstruction during a prolonged inspiratory phase resulted in lesions compatible with pulmonary oedema at post-mortem examination [8]. In 1989 and 1995, two case series described the development of pulmonary oedema in conscious dogs due to UAO resulting from laryngeal

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paralysis, laryngeal oedema or obstructive airway masses [9,10]. Another case series was recently published describing the radiographic appearance of 23 cases with presumed post-obstructive pulmonary oedema in conscious dogs [5].

To the authors knowledge this is the first case report in the veterinary literature describing the pathophysiology, critical care and management of post-anaesthetic NPPO in a dog.

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CASE PRESENTATION ***Presenting features, clinical and environmental history***

A four-month-old, 11.6 kg, body condition score 6/9 [11], female English Bulldog was presented for investigation and management of chronic urinary incontinence of one-month duration. At presentation the patient was bright and alert. Clinical examination revealed a recessed vulva and

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urine-stained fur in the peri-vulvar area. Thoracic auscultation was unremarkable, respiratory rate was 32 rpm and no obvious BOAS was detected. Cardiac auscultation was unremarkable (no murmurs detected) and the heart rate was 140 bpm with regular rhythm. Temperature recorded was 38ºC. Blood haematology and serum biochemistry were unremarkable. An American Society of Anaesthesiology (ASA) physical status classification of 2 was assigned to the dog [12]. A Computed Tomography (CT) scan of the thorax and abdomen, under sedation, was scheduled for the same day. The patient was premedicated with 0.01mg/kg medetomidine (Medetor, Virbac) and 0.2mg/kg butorphanol (Dolorex, MSD Animal Health) by intramuscular injection. A 22 gauge intravenous cannula was placed aseptically in the left cephalic vein. Oxygen was supplemented via face mask throughout the sedation period at a flow rate of 4L/min. Fluid therapy was initiated, before CT contrast was administered, with Hartmann's Solution (Aqupharm 11, Animacare) at a rate of 4mL/kg/hr. Pulse oximetry, non-invasive oscillometric blood pressure measurement, pulse rate and respiratory rate were monitored using a multiparameter monitor (Datex-Ohmeda S/5, GE Healthcare).

CT examination of the abdomen following intravenous injection of contrast medium revealed dilation of the urethra with absence of normal vesiculourethral junction and mild dilation of the left ureter.

A retrograde vaginourethrogram was ~~immediately~~ performed under general anaesthesia~~,~~ immediately after the CT scan. Propofol 2mg/kg (PropoFlo Plus, Zoetis) was administered intravenously. The trachea was intubated using a cuffed (high volume, low pressure) 8 mm inner diameter polyvinyl chloride (PVC) ETT. No difficulties were encountered during tracheal intubation although the ETT was found to be close-fitting as no cuff inflation was required when leak testing ~~the system~~. General anaesthesia was maintained with sevoflurane (SevoFlo, Zoetis) vaporised in 100 per cent oxygen. Anaesthetic monitoring included electrocardiography, pulse oximetry, capnography and noninvasive oscillometric blood pressure measurement using a multiparameter monitor (DatexOhmeda S/5, GE Healthcare). The trachea was extubated as soon as the patient swallowed, no complications were detected at that time, and no fluid or foam were visualised in the ETT. There were no breathing difficulties or signs of gastroesophageal reflux (GOR) detected after extubation. The patient was hypothermic in the recovery period (35.9ºC). In order to treat the hypothermia active warming was initiated with an active warming device (Hot Dog Patient Warming; Augustine Surgical Inc) and further temperature measurements were performed until the hypothermia resolved three hours after extubation. The patient was kept on intravenous fluid therapy for fifteen hours at a rate of 4ml/kg/hr, using a fluid pump, in order to avoid CT contrast induced nephropathy [13]. Fluid therapy guidelines suggest maintenance fluid rates between 2-6 ml/kg/hr in healthy dogs [14]. Well-hydrated patients with normal renal and heart function are generally able to regulate and excrete this fluid volumes. Although unlikely, this fluid therapy

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regime may have predisposed the patient to volume overload.

The animal was hospitalised overnight and was examined every four hours. The patient was considered clinically normal for the last time at 4am. At 8 am, fourteen hours after general anaesthesia, clinical examination of the patient revealed coughing, respiratory distress with a marked increase in inspiratory effort and a respiratory rate of 40 rpm. During thoracic auscultation increased upper respiratory sounds and wheezes were heard ~~and~~. ~~n~~No crackles were noticed. On cardiac auscultation, no heart murmur was heard, the patient had a regular heart rhythm, the heart rate was 124 bpm, mucous membranes were pink and moist, and the capillary refill time was one second. Rectal temperature measured was 38,7ºC. Urgent thoracic radiographs were performed to establish the origin of the sudden onset of respiratory distress. The possibility of regurgitation followed by aspiration and subsequent pneumonia was suspected.

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INVESTIGATIONS ***If relevant***

In order to perform radiographs, the patient was sedated with 0.001mg/kg medetomidine (Medetor, Virbac) and 0.2mg/kg butorphanol (Dolorex, MSD Animal Health) intravenously. Dorsoventral and lateral inspiratory thoracic radiographs were obtained (Fig.1). A generalised increase in soft tissue and ground glass opacities of the pulmonary parenchyma was identified, associated with multiple air bronchograms (unstructured interstitial and alveolar lung patterns). The pulmonary lesions were more severe in the perihilar region and reduced in severity towards the periphery. The border of the cardiac silhouette was partially effaced by the neighbouring lung changes, but the cardiac silhouette was not enlarged. Retrospectively, the CT of the caudal thorax earlier performed revealed no abnormalities in the caudal two thirds of the lungs. Tracheal inner diameter measured 8.92mm and thoracic inlet measurement 6.67cm. The tracheal ~~:~~ thoracic inlet ratio was within normal limits for a English Bulldog ~~(0.134)~~ [15,16].

Due to the more severe pulmonary lesions in the perihilar region suggesting the possibility of cardiogenic pulmonary oedema, a single dose of furosemide at 2mg/kg was administered intravenously promptly and an echocardiography was performed. Neither left nor right atrial enlargement was identified and systolic function appeared normal. There were no valvular regurgitations and no evidence of increased filling pressures detected; therefore, cardiogenic cause of pulmonary oedema was discarded.

The pharynx and the larynx were visually examined using ~~:~~ a laryngoscope ~~with a light source with~~while the animal was profoundly sedated. The larynx was ~~found to be~~ grossly inflamed with erythema and swelling of the area. No mass, foreign body, laryngeal paralysis or other source of UAO was

identified during examination.

DIFFERENTIAL DIAGNOSIS *If relevant*

From the history, presentation and radiographic findings a non-cardiogenic pulmonary oedema was highly suspected. Alternative differential diagnoses included idiopathic interstitial pneumonia, neoplastic infiltration or non-witnessed aspiration pneumonia.

A presumptive diagnosis of post-anaesthetic NPPO was made.

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TREATMENT ***If relevant***

The dog was transferred to the intensive care unit. The patient showed laboured breathing and a significant stertor could be heard. Positioning the patient with the neck extended significantly improved ~~the~~ her level of comfort. A continuous rate infusion of butorphanol (Dolorex; MSD Animal Health) at 0.2mg/kg/hr was started to provide sedation, analgesia and antitussive therapy with minimal respiratory depression [17,18]. Oxygen supplementation via nasal prongs was implemented at a flow rate of 1.5L min^{-1}. Saturation of haemoglobin with oxygen was monitored using a portable pulse oximeter (Radical 7 Pulse Oximeter; Masimo). No episodes of ~~patient's~~ desaturation were reported, ~~pulse oximeter~~oxygen haemoglobin saturation values were always above 95% of saturation of haemoglobin with oxygen.

Salbutamol nebulization therapy (Ventolin: Glaxo Smith Klein) was initiated at a dose of 0.035 mg/kg TID administered via metered dose inhalers over periods of 6 breaths using an aerosol chamber with a fitted face mask (AeroDawg; Truddel Medical International).

Therapy with dexamethasone (0.2mg/kg IV SID) (Colvasone, Norbook); omeprazole (1mg/kg IV BID) (Omeprazole; Star Pharmaceuticals Ltd.); and cefuroxime (20mg/kg IV TID) (Zinacef; GlaxoSmithKlein) was initiated due to the possibility of regurgitation followed by aspiration and subsequent pneumonia as a potential differential diagnosis at the time.

OUTCOME AND FOLLOW-UP

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The animal responded well to treatment. Sixteen hours after the initial clinical signs, the patient was bright and alert. Respiratory rate decreased (20 rpm), no cough or increased inspiratory effort was detected. All medications were discontinued 36 hours after recognition of the clinical signs. The animal was discharged from the hospital 48 hours after this event. Unfortunately, no follow up imaging was performed.

Six months after discharge the animal has fully recovered from this episode with no complications arising from the NPPO.

DISCUSSION ***Include a very brief review of similar published cases***

DIFFERENTIAL DIAGNOSIS

The possibility of aspiration and secondary pneumonia was initially suspected before diagnostic imaging was performed. In anaesthetised dogs, gastric oesophageal reflux (GOR) has a high

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incidence, which ranges from 16 per cent[19] to 55 per cent[20]. A clinical trial showed a higher incidence of GOR (60 per cent vs 40 per cent) when comparing anaesthetised brachycephalic and non-brachycephalic dogs, although ~~this~~ the difference was not statistically significant[21]. This is, in part, related to the high negative intrathoracic pressures generated to overcome the upper respiratory tract obstruction [22–24]. GOR is associated with an increased risk of aspiration and secondary pneumonia [22,24].

In ~~this case~~the case reported here and with hindsight, we can exclude~~excluded~~ the possibility of aspiration pneumonia as the cause of the pulmonary oedema due to the rapid resolution of the clinical signs. Two studies reflected on the duration of ~~hospitalization~~ hospitalisation for dogs with aspiration pneumonia and resolution of clinical signs. Results showed in these studies ranged from 3 to 5 days of hospitalization in the intensive care unit for dogs recovering from aspiration pneumonia [25,26].

~~In terms of radiography~~Moreover, there are different radiographic appearances when comparing NPPO to aspiration pneumonia. In aspiration pneumonia the most gravity dependent areas are the most frequently affected[27]~~. The positioning of the patient during aspiration may predict the location of pulmonary infiltrates.~~ In sternal recumbency it is more likely that the right lung is affected, as the right mainstem bronchus is a more direct prolongation of the trachea than the left. In ventrodorsal positioning the caudal lung lobes seem to be more affected [28]. A recent case series focused on the radiographic appearance of non-cardiogenic pulmonary oedema suggested that a dorsal distribution of the lung lesions seemed to be more often observed in NPPO than in other causes of non-cardiogenic pulmonary oedema, although, the authors could not give an explanation

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to this finding[5].

In dogs with experimentally induced lung aspiration, radiographic signs were only seen 24 hours post aspiration and clinical signs of cough and respiratory distress were only present two days after the event [28]. In this case, clinical signs and radiographic changes occurred between ten to fourteen hours after extubation, ~~although aspiration before sedation cannot be excluded~~. Also, abnormal radiographic findings were mainly caudodorsally located which differs from cases of aspiration pneumonia.

In human medicine, ~~this~~ post-anaesthetic ~~complication~~ NPPO has a variable onset of clinical signs, ~~it may~~which may vary from few minutes to several hours (up to 24 hours) following extubation or relief of obstruction [2,29,30]. Delayed onset of laryngeal oedema due to trauma has been reported as a complication of the surgical treatment of BOAS in dogs[31]. In one case series, four dogs developed laryngeal oedema post-surgery. The onset of clinical signs of upper airway obstruction, such as increased respiratory effort and cyanosis, were noted one, three, seven and ten hours after surgery. The authors mentioned that the laryngeal oedema could have resulted from surgery trauma or induced by the ETT[31].

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Other causes of non-cardiogenic pulmonary oedema, such as direct lung injury (fire smoke exposure, toxin inhalation); neurogenic oedema (electrocution); systemic disease (neoplasia, uremic syndrome, pancreatitis); near drowning; blood transfusion; anaphylaxis[5] were also discarded by clinical history, clinical examination and blood analysis. Neurogenic oedema due to seizures is difficult to completely exclude as the animal was not constantly monitored overnight and a seizure episode cannot be completely excluded. Although, to date, no history or clinical signs of neurologic disease have been reported in this patient, therefore the main causes of neurogenic pulmonary oedema were considered unlikely.

CONTRIBUTION FACTORS FOR THE DEVELOPMENT OF NPPO

PATHOPHYSIOLOGY

It is believe that the animal described here suffered from type 1 post-obstructive pulmonary oedema, due to a suspected upper airway obstruction caused by gross swelling and erythema of the larynx. This may have been exacerbated from suspected trauma during tracheal intubation with an oversized ETT. A recent study in Beagles suggested that a suitably sized ETT for dogs should measure 70% of the internal tracheal diameter measured on thoracic radiography[32]. In this particular case, the measurement using the same method revealed 8.92mm internal tracheal diameter which corresponds to a 6.2mm ETT. An 8mm ETT was used to intubate the trachea of this patient, which could potentially explain the laryngeal swelling, erythema and secondary post extubation UAO.

BOAS

~~BOAS has an impact on the management of these patients during anaesthesia and recovery~~ [22]. BOAS is characterised by dynamic and/or static UAO[33]. ~~These~~ patients suffering from this syndrome are subjected to an increased resistance to inspiratory airflow which results in increased inspiratory effort and the generation of supraphysiologic negative thoracic and airway pressures [33]. In severe cases of BOAS, UAO can result in NPPO [22]. In our patient brachycephalic conformation may have played a role in aggravating the UAO.

SEDATION

~~This animal was sedated with a low dosage of medetomidine to safely perform the radiographs and the echocardiography.~~ In cases of NPPO, α_2-agonists must be used with caution. Profound sedation with this class of drugs induces recumbency, reduces pharyngeal muscle tone and may predispose to hypoventilation. All of these factors can theoretically worsen any UAO already present [22,34]. On the other hand, sedation may be useful in controlling excessive panting associated with stress, reducing further airway swelling or collapse and decreasing oxygen consumption[22]. This animal was sedated with a low dosage of medetomidine to safely perform the radiographs and the echocardiography. This patient was closely monitored for signs of UAO including increased stertor/stridor, increased inspiratory effort and exaggerated movement of the chest wall.

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Elevating the patient's head improved the audible stertor/stridor during sedation. Oxygen was supplemented via face mask and haemoglobin saturation with oxygen was monitored via pulse oximetry at all times during this process. ~~If necessary~~ ~~antipamezole~~ ~~could have been administrated in this case, as this α_2-antagonist counteracts the respiratory depression caused by the administration of α_2-agonists~~ [35,36]. Butorphanol can be used to provide sedation, analgesia and antitussive therapy with minimal respiratory depression in cases of respiratory distress and was used successfully [17,18].

PAEDIATRIC PATIENT

The fact that this was a paediatric patient may have played a role in the development of pulmonary oedema in this case. Young animals have a smaller functional residual capacity, therefore they will quickly develop hypoxia in the event of an UAO [37,38]. The rib cage of young animals is very compliant, resulting in less competent ventilation and greater work of breathing. This may predispose paediatric patients to hypoxia and ventilatory fatigue, which can be aggravated in the event of an UAO[38]. The larynx of puppies is delicate, and extreme care should be taken to intubate the trachea atraumatically [37]. This patient was 4 months old and intubation of the trachea was performed with an oversized ETT which potentially caused the laryngeal oedema, which was theorised to be the cause of the UAO. ~~Hypoxia may have developed quicker in this patient for the reasons described above.~~

TREATMENT

The priorities in patients presenting NPPO are to relieve the UAO and correct the hypoxaemia. Supportive care should be implemented ~~aiming~~ to maintain a patent airway and ~~ensuring~~ ensure adequate oxygenation [2,39]. Oxygen supplementation, continuous positive airway pressure (CPAP), intermittent positive pressure ventilation (IPPV) and positive end-expiratory pressure (PEEP) are methods ~~used~~ described to fulfil those goals. Other medications such as glucocorticoids and β_2-

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agonists are also used to ~~minimize~~ minimise the impact of the UAO.

OXYGEN SUPPLEMENTATION

Traditional oxygen therapy is most usually provided via a face mask, nasal prongs or oxygen cage, delivering dry, cold oxygen with FIO_2 of 40 to 70% at flow rates of 50–150 mL/kg/min [40]. In a research project including twenty healthy dogs, the mean partial pressure of oxygen (PaO_2) in arterial samples taken after face mask oxygen supplementation was 371.3 mmHg compared to the control group composed by dogs breathing room air (82.43 mmHg) [40]. Passive oxygen administration via a nasal prongs was chosen in this case to provide oxygen to the patient. Unfortunately, no arterial blood gas analysis was performed; this could have provided more reliable information regarding the haemoglobin saturation with oxygen and PaO2.

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CPAP

CPAP is a mode of ventilation used in spontaneously breathing subjects. This is used in humans

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for the treatment of NPPO and sleep apnoea[2,41] . The objective of CPAP is to maintain a positive pressure in the airways during inspiration and expiration. ~~This~~ The intrathoracic positive pressure ~~at the end of expiration will~~ improves alveolar ventilation and re-expand flooded alveoli, promoting the fluid to return to the interstitial space [42]. Other benefits of CPAP include a reduction in preload due to an increase in intrathoracic pressure and a reduction in afterload, via an increase in pericardial pressure and reduction in transmural pressure [42]. It also improves oxygenation, gas exchange, vital signs and reduces work of breathing [43,44]. One of the advantages of CPAP delivery is that there is no need for tracheal intubation and mechanical ventilation. No CPAP delivering device~~s~~ ~~have~~ has been specifically designed for veterinary patients. Two human interfaces for CPAP delivery have been studied in dogs, [45,46]. In healthy sedated dogs, when comparing CPAP via face mask with traditional oxygen therapy delivered via regular face mask, CPAP increased PaO_2 by 102 mmHg and was well tolerated by the patients [45]. Some ~~D~~disadvantages have been highlighted in a research project testing three methods of non-invasive CPAP delivery (custom-made mask, conical face mask and helmet): significant leaks were found when CPAP was delivered to sedated dogs. There is a significant risk of rebreathing and hypoxaemia when CPAP was not maintained. The authors concluded that animals should always be supervised during administration of CPAP [47]. In our patient this method of ventilation was not used because it was not available. ~~at the time, I~~in our opinion it would have been a valid option for treatment of this patient ~~because it would maintain a patent airway, improved oxygenation and reduced the work of breathing. Nevertheless, the temperament of the animal could have limited the use of CPAP in this case.~~

IPPV

IPPV with PEEP has been used in veterinary medicine for treatment of non-cardiogenic pulmonary oedema [48]. The application of PEEP counterbalances the hydrostatic forces leading to pulmonary oedema, redistributing the extravascular fluid from the alveoli into perivascular interstitium and maintaining airway patency [49]. PEEP also improves gas exchange and recruits alveolar units. Application of PEEP up to 13 cmH2O improved alveolar gas exchange in experimentally induced canine pulmonary oedema [50,51]. In this case IPPV and PEEP were not used because this would require endotracheal intubation which could have perpetuated the laryngeal inflammation already present. In human patients with NPPO, IPPV and PEEP are only implemented in severe cases of hypoxaemia, ventilation/perfusion mismatch and poor lung compliance[2]. IPPV and PEEP may present disadvantages when compared to other methods of ventilation such as CPAP. These included: an increased risk of morbidity and mortality; the development of pneumonia, volutrauma and barotrauma; requirements for expensive and specialised equipment and staff; higher costs of patient management in an ICU setting [45,52].

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FUROSEMIDE

In patients suffering from fluid overload, diuretics may play a part in the resolution of pulmonary

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oedema, but in other cases ~~their role~~its indication remains uncertain [53,54]. ~~The reasoning behind using diuretics in these cases is~~Diuretics can be administered ~~to~~i in an attempt to decrease the intravascular volume and alter Starling's equation in favour of intra-capillary filtration and oedema resolution [30]. In our patient Furosemide was administered after radiographs confirmed pulmonary oedema. We had a concern that our patient may have been fluid overloaded, as she received fluid therapy at a rate of 4ml/kg/hr for a period of fifteen hours. The echocardiography discarded that possibility as well as cardiogenic pulmonary oedema.

Therefore the use of furosemide could have been avoided in this particular case.

CORTICOSTEROIDS

Upper airway inflammation is associated with airway narrowing and obstruction. This increases airway resistance, may perpetuate inflammation and worsen coughing episodes. In the ~~short term~~short-term glucocorticoids may be useful in animals with BOAS with pharyngeal or laryngeal swelling[55]. ~~Glucocorticoids were~~Dexamethasone was used in ~~this~~ our case after examination of the larynx, to decrease the inflammation detected in that area.

SALBUTAMOL

~~β_2-agonists may be useful in lower airway disease in dogs[55].~~ The use of β_2-agonists is current practice in the treatment of NPPO in human medicine[59]In human medicine, aerosolis~~z~~ed salbutamol was found to accelerate the resolution of pulmonary oedema, improve blood oxygenation, and stimulate cardiovascular function after lung lobe resection[56]. β_2-agonists could potentially increase the rate of alveolar fluid clearance through increased active cation transport, which may well accelerate the resolution of the clinical signs of pulmonary oedema[57,58]. ~~The use of β_2-agonists is current practice in the treatment of NPPO in human medicine[59]~~.Furthermore Interstitial oedema may induce narrowing of the bronchial lumen. This can be detected on thoracic auscultation as wheezing sounds[57]. In our case, clear wheezing was detected on thoracic auscultation; therefore, ~~nebulisation~~ bronchodilation with salbutamol was initiated.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

- Endotracheal intubation should be performed atraumatically with an appropriately sized ETT (in length and diameter). When intubating the trachea of a patient correct position of the patient, use of laryngoscope (which provides adequate light and ~~visualization~~ visualisation of the larynx) and appropriate depth of anaesthesia are extremely important to avoid complications.
- Delayed onset of laryngeal oedema resulting in NPPO is possible~~;~~. therefore animals should be closely monitored in the post-operative period.
- NPPO ~~is a potential complication in the pre-anaesthetic period and~~ can be treated with oxygen supplementation, corticosteroids and short-acting β_2-agonists.

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- Early recognition of the clinical signs and establishment of a prompt diagnosis is extremely important in the outcome of the case.

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FIGURE/VIDEO CAPTIONS ***figures should NOT be embedded in this document***

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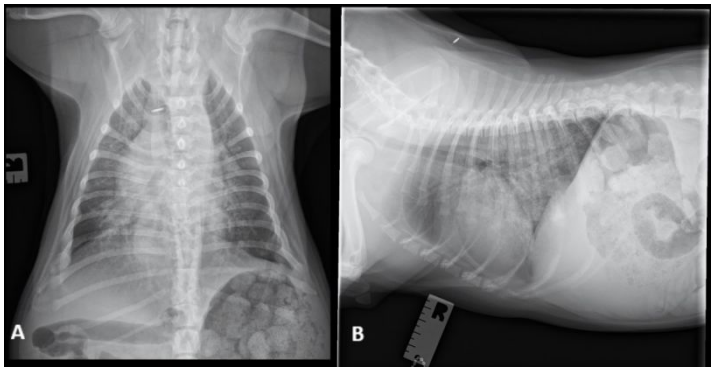

Fig.1. (A) Dorsoventral thoracic radiograph during inspiration. (B) Right lateral thoracic radiograph during inspiration. In these images it is possible to identify a generalised increase in soft tissue and ground glass opacities of the pulmonary parenchyma, associated with multiple air bronchograms. The pulmonary lesions are more severe in the perihilar region and reduced in severity towards the periphery. The border of the cardiac silhouette was partially effaced by the neighbouring lung changes, but the cardiac silhouette was not enlarged.

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TITLE OF CASE ***Do not include "a case report"***
POSTOBSTRUCTIVE NEGATIVE PRESSURE PULMONARY OEDEMA IN A DOG
SUMMARY ***Up to 150 words summarising the case presentation and outcome (this will be freely available online)***

A four-month-old English bulldog was anaesthetised for investigation and management of chronic urinary incontinence. In the post-anaesthetic period the patient developed respiratory distress, with marked cough and increased inspiratory effort. Diagnostic imaging suggested pulmonary oedema. After excluding all other causes of cardiogenic and non-cardiogenic pulmonary oedema it was hypothesised that the patient developed post-anaesthetic negative pressure pulmonary oedema, suspected to have been exacerbated by tracheal intubation with an oversized endotracheal tube leading to laryngeal swelling and obstruction. The animal was treated with oxygen supplementation, corticosteroids and β-2 adrenergic receptor agonists. The patient recovered from the event and was discharged from the hospital after forty-eight hours. This article discusses in further details other management options of negative pressure pulmonary oedema. This is the first case report discussing the pathophysiology, critical care and management of post-anaesthetic negative pressure pulmonary oedema in a dog.

BACKGROUND ***Why you think this case is important – why did you write it up?***

Pulmonary oedema is defined as an abnormal accumulation of fluid in the extravascular tissues and spaces of the lung that occurs when the lymphatic circulation is unable to drain the excessive fluid present in the extravascular space [1].

Post-obstructive pulmonary oedema can be subdivided into two types: Type 1 which is associated with an increase in inspiratory effort due to an acute upper airway obstruction (UAO) and type 2 which results from a relief of a chronic partial UAO (e.g. after laryngeal mass resection) [2]. Postobstructive pulmonary oedema type 1 is also known as negative pressure pulmonary oedema (NPPO) and has been highlighted as a potential complication in the post-anaesthetic period in people and horses[3,4]. Multiple causes have been attributed to the development of NPPO: brachycephalic obstructive airway syndrome (BOAS), strangulation, choking, near drowning, airway collapse, laryngeal mass, laryngeal paralysis, endotracheal tube (ETT) obstruction, laryngospasm and partial occlusion of the upper airway tract with a foreign body or other mass [2,5].

now accepted that this multifactorial process involving negative pressures and hypoxia[2]. The pathophysiologic mechanism behind NPPO was primarily described in the 1940s [6] and it is is a

Physiologically the UAO creates a large negative transpulmonary and interpleural pressure gradient favouring movement of fluid from the capillaries through the alveolar capillary barrier into the extravascular space [3]. This increase in hydrostatic pressures and oedema formation in the lungs [2,7], contributes to the overall translocation of fluid from the capillaries into the alveolar spaces.

In the veterinary literature few reports have been published discussing this event. In 1927, a research article reporting the response to respiratory resistance in dogs found that a partial fixed obstruction during a prolonged inspiratory phase resulted in lesions compatible with pulmonary oedema at post-mortem examination [8]. In 1989 and 1995, two case series described the development of pulmonary oedema in conscious dogs due to UAO resulting from laryngeal paralysis, laryngeal oedema or obstructive airway masses [9,10]. Another case series was recently published describing the radiographic appearance of 23 cases with presumed post-obstructive pulmonary oedema in conscious dogs [5].

To the authors knowledge this is the first case report in the veterinary literature describing the

pathophysiology, critical care and management of post-anaesthetic NPPO in a dog.

CASE PRESENTATION ***Presenting features, clinical and environmental history***

A four-month-old, 11.6 kg, body condition score 6/9 [11], female English Bulldog was presented for investigation and management of chronic urinary incontinence of one-month duration. At presentation the patient was bright and alert. Clinical examination revealed a recessed vulva and

urine-stained fur in the peri-vulvar area. Thoracic auscultation was unremarkable, respiratory rate

was 32 rpm and no obvious BOAS was detected. Cardiac auscultation was unremarkable (no murmurs detected) and the heart rate was 140 bpm with regular rhythm. Temperature recorded was 38ºC. Blood haematology and serum biochemistry were unremarkable. An American Society of Anaesthesiology (ASA) physical status classification of 2 was assigned to the dog [12]. A Computed Tomography (CT) scan of the thorax and abdomen, under sedation, was scheduled for the same day. The patient was premedicated with 0.01mg/kg medetomidine (Medetor, Virbac) and 0.2mg/kg butorphanol (Dolorex, MSD Animal Health) by intramuscular injection. A 22 gauge intravenous cannula was placed aseptically in the left cephalic vein. Oxygen was supplemented via face mask throughout the sedation period at a flow rate of 4L/min. Fluid therapy was initiated, before CT contrast was administered, with Hartmann's Solution (Aqupharm 11, Animacare) at a rate of 4mL/kg/hr. Pulse oximetry, non-invasive oscillometric blood pressure measurement, pulse rate and respiratory rate were monitored using a multiparameter monitor (Datex-Ohmeda S/5, GE Healthcare).

CT examination of the abdomen following intravenous injection of contrast medium revealed dilation of the urethra with absence of normal vesiculourethral junction and mild dilation of the left ureter.

A retrograde vaginourethrogram was immediately performed under general anaesthesia, after the CT scan. Propofol 2mg/kg (PropoFlo Plus, Zoetis) was administered intravenously. The trachea was intubated using a cuffed (high volume, low pressure) 8 mm inner diameter polyvinyl chloride PVC) ETT. No difficulties were encountered during tracheal intubation although the ETT was (found to be close-fitting as no cuff inflation was required when leak testing the system. General anaesthesia was maintained with sevoflurane (SevoFlo, Zoetis) vaporised in 100 per cent oxygen. Anaesthetic monitoring included electrocardiography, pulse oximetry, capnography and noninvasive oscillometric blood pressure measurement using a multiparameter monitor (DatexOhmeda S/5, GE Healthcare). The trachea was extubated as soon as the patient swallowed, no complications were detected at that time, and no fluid or foam were visualised in the ETT. There were no breathing difficulties or signs of gastroesophageal reflux (GOR) detected after extubation. The patient was hypothermic in the recovery period (35.9ºC). In order to treat the hypothermia active warming was initiated with an active warming device (Hot Dog Patient Warming; Augustine Surgical Inc) and further temperature measurements were performed until the hypothermia resolved three hours after extubation The patient was kept on intravenous fluid therapy for fifteen hours at a rate of 4ml/kg/hr, using a fluid pump, in order to avoid CT contrast induced nephropathy [13]. Fluid therapy guidelines suggest maintenance fluid rates between 2-6 ml/kg/hr in healthy dogs [14]. Well-hydrated are generally able to regulate and excrete this fluid volumes. Although unlikely, this fluid therapy

patients with normal renal and heart function

Page 3 of 16

regime may have predisposed the patient to volume overload. 8
The animal was hospitalised overnight and was examined eve am, fourteen hours after
considered clinically normal for the last time at 4am. At
general
marked increase in inspiratory effort and coughing, respiratory distress with a
anaesthesia, clinical examination of the patient revealed a
auscultation increased upper respiratory sounds and wheeze atory rate of 40 rpm. During thoracic
noticed. On cardiac auscultation, no heart murmur was heard, t
the heart rate was 124 bpm, mucous membranes were pink an
was one second. Rectal temperature measured was 38,7ºC.
performed to establish the origin of the sudden onset of res
regurgitation followed by aspiration and subsequent pneumon

INVESTIGATIONS ***If relevant***

In order to perform radiographs, the patient was sedated with 0.001mg/kg medetomidine (Medetor, Virbac) and 0.2mg/kg butorphanol (Dolorex, MSD Animal Health) intravenously. Dorsoventral and lateral inspiratory thoracic radiographs were obtained (Fig.1). A generalised increase in soft tissue and ground glass opacities of the pulmonary parenchyma was identified, associated with multiple air bronchograms (unstructured interstitial and alveolar lung patterns). The pulmonary lesions were more severe in the perihilar region and reduced in severity towards the periphery. The border of the cardiac silhouette was partially effaced by the neighbouring lung changes, but the cardiac silhouette was not enlarged. Retrospectively, the CT of the caudal thorax earlier performed revealed no abnormalities in the caudal two thirds of the lungs. Tracheal inner diameter measured 8.92mm and thoracic inlet measurement 6.67cm. The trachea : thoracic inlet ratio was within normal limits for a English Bulldog (0.134) [15,16].

Due to the more severe pulmonary lesions in the perihilar region suggesting the possibility of cardiogenic pulmonary oedema, a single dose of furosemide at 2mg/kg was administered intravenously promptly and an echocardiography was performed. Neither left nor right atrial enlargement was identified and systolic function appeared normal. There were no valvular regurgitations and no evidence of increased filling pressures detected; therefore, cardiogenic cause of pulmonary oedema was discarded.

The pharynx and the larynx were visually examined using laryngoscope with a light source with the animal profoundly sedated. The larynx was found to be grossly inflamed with erythema and swelling of the area. No mass, foreign body, laryngeal paralysis or other source of UAO was

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identified during examination.

DIFFERENTIAL DIAGNOSIS ***If relevant***

From the history, presentation and radiographic findings a non-cardiogenic pulmonary oedema was highly suspected. Alternative differential diagnoses included idiopathic interstitial pneumonia, neoplastic infiltration or non-witnessed aspiration pneumonia.

A presumptive diagnosis of post-anaesthetic NPPO was made.

TREATMENT ***If relevant***

The dog was transferred to the intensive care unit. The patient showed laboured breathing and a significant stertor could be heard. Positioning the patient with the neck extended significantly improved the level of comfort. A continuous rate infusion of butorphanol (Dolorex; MSD Animal Health) at 0.2mg/kg/hr was started to provide sedation, analgesia and antitussive therapy with minimal respiratory depression [17,18]. Oxygen supplementation via nasal prongs was implemented at a flow rate of 1.5L min^{-1}. Saturation of haemoglobin with oxygen was monitored using a portable pulse oximeter (Radical 7 Pulse Oximeter; Masimo). No episodes of patient's desaturation were reported, pulse oximeter values were always above 95% of saturation of haemoglobin with oxygen.

Salbutamol nebulization therapy (Ventolin: Glaxo Smith Klein) was initiated at a dose of 0.035 mg/kg TID administered via metered dose inhalers over periods of 6 breaths using an aerosol chamber with a fitted face mask (AeroDawg; Truddel Medical International).

Therapy with dexamethasone (0.2mg/kg IV SID) (Colvasone, Norbook); omeprazole (1mg/kg IV BID) (Omeprazole; Star Pharmaceuticals Ltd.); and cefuroxime (20mg/kg IV TID) (Zinacef; GlaxoSmithKlein) was initiated due to the possibility of regurgitation followed by aspiration and subsequent pneumonia.

OUTCOME AND FOLLOW-UP

The animal responded well to treatment. Sixteen hours after the initial clinical signs, the patient was bright and alert. Respiratory rate decreased (20 rpm), no cough or increased inspiratory effort was detected. All medications were discontinued 36 hours after recognition of the clinical signs. The animal was discharged from the hospital 48 hours after this event. Unfortunately, no follow up imaging was performed.

Six months after discharge the animal has fully recovered from this episode with no complications arising from the NPPO.

DISCUSSION ***Include a very brief review of similar published cases***

DIFFERENTIAL DIAGNOSIS

The possibility of aspiration and secondary pneumonia was initially suspected before diagnostic imaging was performed. In anaesthetised dogs, gastric oesophageal reflux (GOR) has a high

incidence, which ranges from 16 per cent[19] to 55 per cent[20]. A clinical trial showed a higher incidence of GOR (60 per cent vs 40 per cent) when comparing anaesthetised brachycephalic and non-brachycephalic dogs, although this was not statistically significant[21]. This is, in part, related to the high negative intrathoracic pressures generated to overcome the upper respiratory tract obstruction [22–24]. GOR is associated with an increased risk of aspiration and secondary pneumonia [22,24].

In this case we excluded the possibility of aspiration pneumonia as the cause of the pulmonary oedema due to the rapid resolution of the clinical signs. Two studies reflected on the duration of hospitalization for dogs with aspiration pneumonia and resolution of clinical signs. Results showed in these studies ranged from 3 to 5 days of hospitalization in the intensive care unit for 17 dogs recovering from aspiration pneumonia [25,26].

In terms of radiography, there are different radiographic appearances when comparing NPPO to aspiration pneumonia. In aspiration pneumonia the most gravity dependent areas are the most affected[27]. The positioning of the patient during aspiration may predict the location of pulmonary infiltrates. In sternal recumbency it is more likely that the right lung is affected, as the right mainstem bronchus is a more direct prolongation of the trachea than the left. In ventrodorsal

positioning the caudal lung lobes seem to be more affected [28]. A recent case series focused on the radiographic appearance of non-cardiogenic pulmonary oedema suggested that a dorsal distribution of the lung lesions seemed to be more often observed in NPPO than in other causes of non-cardiogenic pulmonary oedema, although, the authors could not give an explanation to this finding[5].

In dogs with experimentally induced lung aspiration, radiographic signs were only seen 24 hours post aspiration and clinical signs of cough and respiratory distress were only present two days [28]. In this case, clinical signs and radiographic changes occurred between ten to 43 after the event fourteen hours after extubation, although aspiration before sedation cannot be excluded. Also, abnormal radiographic findings were mainly caudodorsally located which differs from cases of aspiration pneumonia. In human medicine, this post-anaesthetic complication has a variable onset of clinical signs, it may vary from few minutes to several hours (up to 24 hours) following extubation or relief of obstruction [2,29,30]. Delayed onset of laryngeal oedema due to trauma has been reported as a complication of the surgical treatment of BOAS in dogs[31]. In one case series, four dogs developed laryngeal oedema post-surgery. The onset of clinical signs of upper airway obstruction, such as increased respiratory effort and cyanosis, were noted one, three, seven and ten hours after surgery. The authors mentioned that the laryngeal oedema could have resulted from surgery trauma or induced by the ETT[31].

Other causes of non-cardiogenic pulmonary oedema, such as direct lung injury (fire smoke exposure, toxin inhalation); neurogenic oedema (electrocution); systemic disease (neoplasia, uremic syndrome, pancreatitis); near drowning; blood transfusion; anaphylaxis[5] were also discarded by clinical history, clinical examination and blood analysis. Neurogenic oedema due to seizures is difficult to completely exclude as the animal was not constantly monitored overnight and a seizure episode cannot be completely excluded. Although, to date, no history or clinical signs of neurologic disease have been reported in this patient, therefore the main causes of neurogenic pulmonary oedema were considered unlikely.

CONTRIBUTION FACTORS FOR THE DEVELOPMENT OF NPPO

PATHOPHYSIOLOGY

It is believe that the animal described here suffered from type 1 post-obstructive pulmonary oedema, due to a suspected upper airway obstruction caused by gross swelling and erythema of the larynx. This may have been exacerbated from suspected trauma during tracheal intubation with an oversized ETT. A recent study in Beagles suggested that a suitably sized ETT for dogs should measure 70% of the internal tracheal diameter measured on thoracic radiography[32]. In this particular case, the measurement using the same method revealed 8.92mm internal tracheal diameter which corresponds to a 6.2mm ETT. An 8mm ETT was used to intubate the trachea of this patient, which could potentially explain the laryngeal swelling, erythema and secondary post extubation UAO.

BOAS

BOAS has an impact on the management of these patients during anaesthesia and recovery [22]. BOAS is characterised by dynamic and/or static UAO[33]. These patients are subjected to an increased resistance to inspiratory airflow which results in increased inspiratory effort and the generation of supraphysiologic negative thoracic and airway pressures [33]. In severe cases of BOAS, UAO can result in NPPO [22]. In our patient brachycephalic conformation may have played a role in aggravating the UAO.

SEDATION

This animal was sedated with a low dosage of medetomidine to safely perform the radiographs and the echocardiography. In cases of NPPO, α_2-agonists must be used with caution. Profound sedation with this class of drugs induces recumbency, reduces pharyngeal muscle tone and may predispose to hypoventilation. All of these factors can theoretically worsen any UAO already present [22,34]. On the other hand, sedation may be useful in controlling excessive panting associated with stress, reducing further airway swelling or collapse and decreasing oxygen consumption[22]. This patient was closely monitored for signs of UAO including increased stertor/stridor, increased inspiratory effort and exaggerated movement of the chest wall.

Elevating the patient's head improved the audible stertor/stridor during sedation. Oxygen was supplemented via face mask and haemoglobin saturation with oxygen was monitored via pulse oximetry at all times during this process. If necessary antipamezole could have been administrated in this case, as this α_2-antagonist counteracts the respiratory depression caused by the administration of α_2-agonists [35,36]. Butorphanol can be used to provide sedation, analgesia and antitussive therapy with minimal respiratory depression in cases of respiratory distress and was used successfully [17,18].

PAEDIATRIC PATIENT

The fact that this was a paediatric patient may have played a role in the development of pulmonary oedema in this case. Young animals have a smaller functional residual capacity, therefore they will quickly develop hypoxia in the event of an UAO [37,38]. The rib cage of young animals is very compliant, resulting in less competent ventilation and greater work of breathing. This may predispose paediatric patients to hypoxia and ventilatory fatigue, which can be aggravated in the event of an UAO[38]. The larynx of puppies is delicate, and extreme care should be taken to intubate the trachea atraumatically [37]. This patient was 4 months old and intubation of the trachea was performed with an oversized ETT which potentially caused the laryngeal oedema, which was theorised to be the cause of the UAO. Hypoxia may have developed quicker in this patient for the reasons described above.

TREATMENT

The priorities in patients presenting NPPO are to relieve the UAO and correct the hypoxaemia. Supportive care should be implemented aiming to maintain a patent airway and ensuring adequate oxygenation [2,39]. Oxygen supplementation, continuous positive airway pressure (CPAP), intermittent positive pressure ventilation (IPPV) and positive end-expiratory pressure (PEEP) are methods used to fulfil those goals. Other medications such as glucocorticoids and β_2-agonists are also used to minimize the UAO.

OXYGEN SUPPLEMENTATION

Traditional oxygen therapy is most usually provided via a face mask, nasal prongs or oxygen cage, delivering dry, cold oxygen with FIO_2 of 40 to 70% at flow rates of 50 –150 mL/kg/min [40].

In a research project including twenty healthy dogs, the mean partial pressure of oxygen (PaO_2) in arterial samples taken after face mask oxygen supplementation was 371.3 mmHg compared to the control group composed by dogs breathing room air (82.43 mmHg) [40]. Passive oxygen administration via a nasal prongs was chosen in this case to provide oxygen to the patient. Unfortunately, no arterial blood gas analysis was performed; this could have provided more reliable information regarding the haemoglobin saturation with oxygen and PaO2.

CPAP

CPAP is a mode of ventilation used in spontaneously breathing subjects. This is used in humans

for the treatment of NPPO and sleep apnoea[2,41]. The objective of CPAP is to maintain a positive pressure in the airways during inspiration and expiration. This intrathoracic positive pressure at the end of expiration will improve alveolar ventilation and re-expand flooded alveoli, promoting the fluid to return to the interstitial space [42]. Other benefits of CPAP include a reduction in preload due to an increase in intrathoracic pressure and a reduction in afterload, via an increase in pericardial pressure and reduction in transmural pressure [42]. It also improves oxygenation, gas exchange, vital signs and reduces work of breathing [43,44]. One of the advantages of CPAP delivery is that there is no need for tracheal intubation and mechanical ventilation. No CPAP delivering devices have been designed for veterinary patients. Two human interfaces for CPAP delivery have been studied in dogs, [45,46]. In healthy sedated dogs, when comparing CPAP via face mask with traditional oxygen therapy delivered via regular face mask, CPAP increased PaO_2 by 102 mmHg and was well tolerated by the patients [45]. Disadvantages have been highlighted in a research project testing three methods of non-invasive CPAP delivery (custom-made mask, conical face mask and helmet): significant leaks were found when CPAP was delivered to sedated dogs. There is a significant risk of rebreathing and hypoxaemia when CPAP was not maintained. The authors concluded that animals should always be supervised during administration of CPAP [47]. In our patient this method of ventilation was not used because it was not available at the time, in our opinion it would have been a valid option for treatment of this patient because it would maintain a patent airway, improved oxygenation and reduced the work of breathing. Nevertheless, the temperament of the animal could have limited the use of CPAP in this case.

IPPV

IPPV with PEEP has been used in veterinary medicine for treatment of non-cardiogenic pulmonary oedema [48]. The application of PEEP counterbalances the hydrostatic forces leading to pulmonary oedema, redistributing the extravascular fluid from the alveoli into perivascular interstitium and maintaining airway patency [49]. PEEP also improves gas exchange and recruits alveolar units. Application of PEEP up to 13 cmH2O improved alveolar gas exchange in experimentally induced canine pulmonary oedema [50,51]. In this case IPPV and PEEP were not used because this would require endotracheal intubation which could have perpetuated the laryngeal inflammation already present. In human patients with NPPO, IPPV and PEEP are only implemented in severe cases of hypoxaemia, ventilation/perfusion mismatch and poor lung compliance[2]. IPPV and PEEP may present disadvantages when compared to other methods of ventilation such as CPAP. These included: an increased risk of morbidity and mortality; the development of pneumonia, volutrauma and barotrauma; requirements for expensive and specialised equipment and staff; higher costs of patient management in an ICU setting [45,52].

FUROSEMIDE

In patients suffering from fluid overload, diuretics may play a part in the resolution of pulmonary

oedema, but in other cases their role remains uncertain [53,54]. The reasoning behind using diuretics in these cases is to attempt to decrease the intravascular volume and alter Starling's equation in favour of intra capillary filtration and oedema resolution [30]. Furosemide was administered after radiographs confirmed pulmonary oedema. We had a concern that our patient may have been fluid overloaded, as she received fluid therapy at a rate of 4ml/kg/hr for a period of fifteen hours. The echocardiography discarded that possibility as well as cardiogenic pulmonary oedema.

Therefore the use of furosemide could have been avoided in this particular case.

CORTICOSTEROIDS

Upper airway inflammation is associated with airway narrowing and obstruction. This increases airway resistance, may perpetuate inflammation and worsen coughing episodes. In the short term glucocorticoids may be useful in animals with BOAS with pharyngeal or laryngeal swelling[55]. Glucocorticoids were used in this case after examination of the larynx, to decrease the inflammation detected in that area.

SALBUTAMOL

β_2-agonists may be useful in lower airway disease in dogs[55]. In human medicine, aerosolized salbutamol was found to accelerate the resolution of pulmonary oedema, improve blood oxygenation, and stimulate cardiovascular function after lung lobe resection[56]. β_2-agonists could potentially increase the rate of alveolar fluid clearance through increased active cation transport, which may well accelerate the resolution of the clinical signs of pulmonary oedema[57,58]. The use of β_2-agonists is current practice in the treatment of NPPO in human medicine[59]. Interstitial oedema may induce narrowing of the bronchial lumen. This can be detected on thoracic auscultation as wheezing sounds[57]. In our case, clear wheezing was detected on thoracic auscultation; therefore, nebulisation with salbutamol was initiated.

LEARNING POINTS/TAKE HOME MESSAGES ***3 to 5 bullet points – this is a required field***

- Endotracheal intubation should be performed atraumatically with an appropriately sized ETT (in length and diameter). When intubating the trachea of a patient correct position of the patient, use of laryngoscope (which provides adequate light and visualization of the larynx) and appropriate depth of anaesthesia are extremely important to avoid complications.
- Delayed onset of laryngeal oedema resulting in NPPO is possible; therefore animals should be closely monitored in the post-operative period.
- NPPO is a potential complication in the pre-anaesthetic period and can be treated with oxygen supplementation, corticosteroids and short-acting β_2-agonists.

 Early recognition of the clinical signs and establishment of a prompt diagnosis is extremely important in the outcome of the case.

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